

water immiscible solvent,

adding to said solution a carboxylic acid in amounts of from 0.75 to 2.0 equivalents per mole of the ethyl 2-dimethylamino-1-phenyl-3-cyclohexene-1-carboxylate, and

stirring the resulting reaction mixture for 0.5 to 2 hours at a temperature of from 50°C to 100°C.

The respective measures are sufficient to eliminate dimethylamine from the 3-dimethylamino-2-phenyl-propionate to obtain the ethyl ester of atropic acid according to the following reaction scheme:



The Examiner's position is, in light of the current wording of Claim 3, not deemed to be well taken. Also, the respective wording is incorporated into Claims 4 to 8 by reference to Claim 3. Favorable reconsideration and withdrawal of the respective rejection is therefore respectfully solicited.

Further, the Examiner rejected Claims 3 to 8 under 35 U.S.C. §103(a) as being unpatentable in light of the teaching of **Novack** (US 3,649,628). For support, the Examiner pointed particularly to the description of Example 1(A) of the reference which comprises

- i) firstly, the preparation of the 3-dimethylamino-4-phenyl-4-carbethoxy- Δ^1 -cyclohexene which is described in col. 6, indicated lines 23 to 37, of the reference,
- ii) subsequently, the separation of the 3-dimethylamino-4-phenyl-4-carbethoxy- Δ^1 -cyclohexene from the reaction mixture which is described in col. 6, indicated lines 38 to 50, of the reference, and
- iii) finally, the isolation of the 3-dimethylamino-4-phenyl-4-carbethoxy- Δ^1 -cyclohexene which is described in col. 6, indicated lines 51 to 60, of the reference.

The separation stage (ii) of **Novack**'s procedure encompasses (1) extracting the cyclohexene base from the benzene based reaction mixture with 1 N hydrochloric acid, (2) basifying the separated aqueous phase, and (3) extracting the cyclohexene base from the basified aqueous phase with petroleum ether.

The Examiner pointed out that the teaching of **Novack** indicates hydrochloric acid and organic acids as being interchangeable, and

argued that an adjustment of molar ranges, pH, time and concentration was a mere routine optimization which was not deemed to impart patentability.

It has to be noted, however, that the reference enumerates hydrochloric acid and other inorganic and organic acids as interchangeable only in the context of medically acceptable acid addition salts of the cyclohexene base.²⁾ No such interchangeability is suggested or even implied in the reference where the separation of the cyclohexene base from the reaction mixture is concerned. Also, it is immediately apparent from the foregoing summary of Example 1(A) of the reference that the extraction of the reaction mixture with hydrochloric acid is conducted not to form a medicinally acceptable salt of the product but to separate the product from other materials which are present in the reaction mixture. The aqueous solution comprising the salt of the cyclohexene base which is obtained after the extraction with hydrochloric acid is subsequently basified, ie. the salt is destroyed, and the base which is liberated again is extracted into petroleum ether. This further corroborates that the extraction with hydrochloric acid cannot reasonably be deemed to serve the preparation of the medicinally acceptable salts which are mentioned in col. 5 of the reference.

A person of ordinary skill in the art would, in light of the foregoing, not have been motivated by the teaching of **Novack** to replace the hydrochloric acid which is employed in the work-up of the reaction mixture by one of the organic acids which are suitable to convert the cyclohexene base into a medically acceptable acid addition salts, as the Examiner would have it.

The teaching of **Novack** not only lacks an incentive for a person of ordinary skill to replace the hydrochloric acid which is employed for extraction of the cyclohexene base from the benzene based reaction mixture by one of the organic acids which may be used to prepare the medicinally acceptable salts which are mentioned in col. 5 of the reference. The reference also lacks any incentive to adjust the amount of the acid which is employed at that stage to an amount of 0.75 to 2 equivalents per mole of the cyclohexene base, or to stir the resulting reaction mixture for a period of 0.5 to 2 hours at a temperature of from 50°C to 100°C, as is required in accordance with applicants' process. It is obviously the goal of **Novack's** extraction

2) Col. 5, indicated lines 11 to 28, of US 3,649,628.

step to remove the cyclohexene base from the reaction mixture as completely as possible. As such, a person of ordinary skill in the art would increase the amounts of the acid which is employed at this stage rather than decreasing the ratio of acid per mole of cyclohexene base.

Three basic criteria have to be met in order to establish a *prima facie* case of obviousness:³⁾

- (1) There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings,
- (2) there must be a reasonable expectation of success, and
- (3) the prior art reference or the combined references must teach or suggest all of the claim limitations.

Additionally, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and cannot be based on the applicant's disclosure.⁴⁾

The description of Example 1(A) and the enumeration of medically suitable salts which are provided by *Novack* clearly fall short from meeting these criteria. Firstly, as explained in the foregoing, the prior art teaching lacks the suggestion or motivation which would have motivated a person of ordinary skill in the art to make the modification which is necessary to arrive at the particular elements of applicants' process. Further, a modification of *Novack*'s extraction step in which the hydrochloric acid is replaced by an organic acid, and/or in which the amount of the acid is adapted to the value specified in applicants' claims, lacks the necessary expectation of success. Organic acids generally exhibit better solubility in organic solvents than inorganic acids. A person of ordinary skill in the art could therefore not reasonably expect that the separation of the cyclohexene base from the benzene based reaction mixture which is sought in accordance with the reference would be successful if the extraction was conducted with an organic acid and/or with acids in an amount of from 0.75 to 2.0 equivalents per mole of the cyclohexene base. Last but not least, the reference fails to teach or suggest the particular measures which are taken in accordance with applicants' process.

3) See MPEP §2143.

4) *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991)

It is therefore respectfully urged that the teaching of *Novack* cannot be deemed to establish that applicants' invention was *prima facie* obvious at the time it was made. Favorable reconsideration of the Examiner's position and withdrawal of the respective rejection is therefore solicited.

In light of the foregoing, the subject matter defined in Claims 3 to 8 is deemed to fully meet the provisions for patentability of the Patent Act, and the application is deemed to be in condition for allowance. Early action by the Examiner would be greatly appreciated by applicants.

REQUEST FOR EXTENSION OF TIME:

It is respectfully requested that a one month extension of time be granted in this case. The respective \$120.00 fee is paid by credit card (Form PTO-2038 enclosed).

Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees, to Deposit Account No. 14.1437. Please credit any excess fees to such deposit account.

Respectfully submitted,

NOVAK DRUCE DELUCA & QUIGG

James Remenick
Reg. No. 36,902

1300 Eye Street, N.W.
Suite 400 East Tower
Washington, D.C. 20005
(202) 659-0100

JR/BAS